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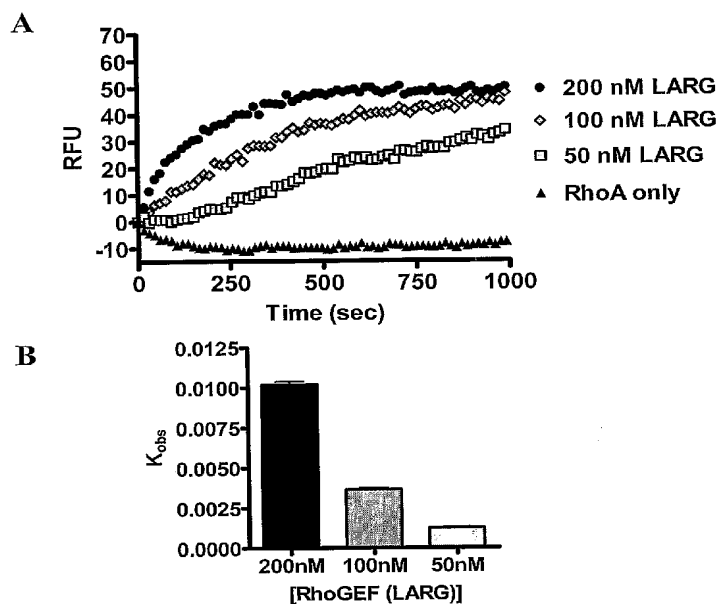
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(54) Title: METHODS FOR IDENTIFYING CHEMICAL MODULATORS OF RAS SUPERFAMILY GTPASE ACTIVITY



(57) Abstract: The present invention provides a method of identifying a compound having the ability to modulate the guanine nucleotide exchange cycle of a Ras superfamily GTPase, comprising: a) contacting the compound with a guanine nucleotide exchange factor and a GTPase and obtaining a baseline fluorescence measurement; b) contacting the guanine nucleotide exchange factor and the GTPase without the compound and obtaining a baseline fluorescence measurement; c) adding a fluorophore-conjugated GTP to the components of (a) and (b), respectively; d) obtaining fluorescence measurements of the respective components of (c) over time; e) subtracting the respective baseline fluorescence measurements of (a) and (b) from each fluorescence measurement of (d); and f) comparing the resulting fluorescence values of (e), wherein a decrease or increase in the rate of fluorescence change with the

compound as compared with the rate of fluorescence change without the compound identifies a compound having the ability to modulate the guanine nucleotide exchange cycle of a Ras superfamily GTPase. Further provided are compounds of the invention and pharmaceutical compositions comprising compounds of the invention useful for the treatment of cancer and neurological disorders.



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